REMARKS

This reply is filed in response to the final Office action mailed July 15, 2010. Claims 1-8, 10 and 12-15 are presented for further examination. Claims 17-21 are withdrawn as a result of a restriction requirement.

Rejection under 35 U.S.C §112, 2nd paragraph

Claim 10 is rejected under 35 U.S.C §112, 2nd paragraph as indefinite. Specifically, the Office asserts that "The claim recites conflicting ranges. Claim 10 depends [from] claim 1, which has the range 20-40%, which conflicts with the 5-20%. Claim 10 does not further limit claim 1." *See* the final Office action, page 2, lines 12-14. Applicants respectfully disagree.

Claim 1 recites that the polyvinyl pyrrolidone (PVP) content [C] in the uppermost layer of a surface on the blood contacting side of the permselective separation membrane is from 20 to 40% by weight. According to the specification, "[t]he content of polyvinyl pyrrolidone in the uppermost layer of the permselective separation membrane is determined from measurement by ESCA .... The ESCA method is typically capable of measuring the polyvinyl pyrrolidone content to a depth of about 10 nm (100 Å) from the surface." *See* paragraph [0058]; emphasis added. By contrast, claim 10 recites the PVP content in a layer near the surface on blood contacting side of the permselective separation membrane is from 5 to 20% by weight. The specification teaches that "[t]he content of polyvinyl pyrrolidone in the layer near the surface is determined from measurement by surface infrared spectroscopy (ATR method). The ATR method is capable of measuring the polyvinyl pyrrolidone content in a region from the surface to a depth of about 1000 to 1500 nm (1 to 1.5 μm) from the surface." *Id*; emphasis added. In view of the teachings above, it would have been apparent to one skilled in the art that claim 10 recites a layer containing a 5-20 wt% PVP content that is different from the layer containing a 20-40 wt% PVP content recited in claim 1. Thus, the 5-20 wt% PVP content recited in claim 10 is not in conflict with the 20-40 wt% PVP content recited in claim 1. Further, since claim 10 recites a layer that is not recited in claim 1, it further limits claim 1.

Accordingly, Applicants submit that claim 10 is not indefinite and request withdrawal of this rejection.

Rejection under 35 U.S.C §103(a)

Claims 1-8, 10 and 12-15 are rejected under 35 U.S.C §103(a) as obvious from Shimagaki et al., U.S. Patent No. 6,103,117 ("Shimagaki").

Independent claim 1 is discussed first. Claim 1, as amended, recites a separation membrane that has the following features:

> (a) the separation membrane is made mainly of a polysulfone-based polymer and polyvinyl pyrrolidone, where a ratio [D]/[C] between the polyvinyl pyrrolidone content [D] in the uppermost layer of a surface on non-blood contacting side and the polyvinyl pyrrolidone content [C] in the uppermost layer of a surface on blood contacting side is 1.1 or higher, wherein the polyvinyl pyrrolidone content [C] in the uppermost layer of a surface on the blood contacting side of the permselective separation membrane is from 20 to 40% by weight and wherein the polyvinyl pyrrolidone content [D] in the uppermost layer of a surface on non-blood contacting side of the permselective separation membrane is from 25 to 50% by weight; and
> (b) when bovine blood at a temperature of 37°C having hematocrit value of 30% and containing 6 to 7 g/dl of total proteins and sodium citrate is flowed through a module containing the separation membrane at a flow rate of 200 ml/min. and a filtration rate of 20 ml/min.:
>
> (i) a sieving coefficient of albumin [A] becomes not less than 0.01 and not more than 0.1 after 15 minutes; and
>
> (ii) a sieving coefficient of albumin [B] becomes not less than 0.005 and less than 0.04 after 2 hours.

According to the specification, the membrane recited in claim 1 can effectively remove α1-microglobulin (which has a molecular weight of 33,000 and is a uremic toxin) from the blood flowing through it, while suppressing the leakage of albumin (which has a molecular weight of 66,000 and is a useful protein) in the blood. *See, e.g.*, paragraphs [0034]-[0036].

The Office does not dispute that Shimagaki does not disclose a membrane having both features (a) and (b) recited in claim 1 as the Office has withdrawn the anticipation rejection based on Shimagaki raised in the last Office action. The Office now asserts that claim 1 would have been obvious from this reference. However, there is nothing in Shimagaki that would have prompted one skilled in the art to modify the membrane described therein to obtain the membrane recited in claim 1. Nor has the Office provided any reason to do so other than improper hindsight.

The Office asserts that

> [t]he declaration presented show some evidence that this ratio [i.e., [D]/[C]] in the reference is in the range of 0.9-1.0. However, this ratio appears to have no criticality and applicant has failed to show any criticality of this ratio. Therefore, the reference membrane is deemed as an obvious equivalent to the claimed membrane.

See the final Office action, page 4, 1st paragraph. However, the specification clearly teaches that

> the present inventors found that the optimum performance of the permselective separation membrane is such that, when assembled into a module, preferably shows the sieving coefficient of albumin [A] not less than 0.01 and not more than 0.1 after 15 minutes and the sieving coefficient of albumin [B] not less than 0.005 and less than 0.04 after 2 hours ....

See paragraph [0035]. Further, the specification teaches that

> It can be seen that, when the ratio [D]/[C] is 1.1 or higher, the sieving coefficient of albumin [A] becomes not less than 0.01 and not higher than 0.1, favorably falling within the predetermined range of 0.005 or higher and less than 0.04, so that a stable separation membrane which well balances between albumin and α1-microglobulin is obtained, in Examples 1 to 3. ... it can be easily understood that <u>one of the factors which have great influence</u> is the ratio [D]/[C] being 1.1 or higher since it brings the sieving coefficient of albumin within the predetermined range.

See paragraph [0035]; emphasis added. In view of the above teachings in the specification, it would have been apparent to one skilled in the art that, contrary to the Examiner's assertion, the [D]/[C] ratio recited in claim 1 is <u>a critical factor</u> in achieving the membrane recited in claim 1. Since Shimagaki does not disclose or suggest such a ratio, it does not render claim 1 obvious.

The Office also asserts that "[t]he actual concentration of PVP on the surfaces appears to be more critical to α-1 microglobulin and hydrophilicity than the ratio ...." *See* the final Office action, page 5, 1st paragraph. Applicants do not agree with the Office's assertion. However, Applicants would like to bring to the Office's attention that claim 1 already recites that the PVP content [C] in the uppermost layer of a surface on the blood contacting side of the permselective separation membrane is from 20 to 40% by weight and the PVP content [D] in the uppermost layer of a surface on non-blood contacting side of the permselective separation membrane is

from 25 to 50% by weight. Thus, even assuming that the Office is correct (which Applicants do not concede), claim 1 already recites the critical PVP contents referred to by the Office. Since Shimagaki does not disclose or suggest such PVP contents, it does render claim 1 obvious on this additional, independent ground.

For at least the reasons set forth above, claim 1 would not have been obvious from Shimagaki. As claims 2-8, 10 and 12-15 depend from claim 1, they also would not have been obvious from Shimagaki.

To complete the record, Applicants would like to comment on a statement made in the final Office action. Specifically, the Office asserts that

> The Examiner wishes to point out that the definition of the %PVP content on the inner and outer surfaces of the membrane is unclear. It is suggested that applicant provide clarification about the definition of this %PVP content, that is, whether it is the ratio of PVP/polysulfone, or PVP to total mass of polymer, PVP/(PVP+polysulfone).

See the final Office action, page 5, 3rd paragraph. According to the specification,

> PVP content on the surface was calculated as follows from the measurement of nitrogen (N) and measurement of sulfur (S): … <In the case of PVP-added PSf (polysulfone) membrane> Content (%) of PVP (Hpvp) = 100 × (N × 111) / (N × 111 + S × 442).[1]

See paragraph [0125]. Thus, the specification teaches that the PVP content in the inner or outer surface of a hollow fiber membrane recited in claim 1 can be determined by the following equation: (weight of PVP) / [(weight of PVP) + (weight of polysulfone)]. Applicants, therefore, submit that the term "PVP content" recited in claim 1 is clear.

Conclusion

Applicants submit that this application is now in condition for allowance and request favorable action.

Any circumstance in which Applicants have: (a) addressed certain comments of the Examiner does not mean that Applicants concede other comments of the Examiner; or (b) made

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[1] In this equation, 111 is the molecular weight of poly(vinylpyrrolidone) and 442 is the molecular weight of polysulfsone.

arguments for the patentability of some claims does not mean that there are no other good reasons for the patentability of those claims and other claims.

The $1,110.00 fee for the Petition for Three-Month Extension of Time is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization.

Please apply any other charges to deposit account 06-1050, referencing Attorney's Docket No. 19461-0005US1.

Respectfully submitted,

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